

PATENT
Attorney Docket No. PCI0770B US

Claim Listing:

1-9. (Cancelled)

10. (Currently Amended) A pharmaceutical composition for treating or preventing a disorder or condition selected from autoimmune diseases, rheumatoid arthritis, type I diabetes (recent onset), lupus, inflammatory bowel disease, optic neuritis, psoriasis, multiple sclerosis, polymyalgia rheumatica, uveitis, and vasculitis, acute and chronic inflammatory conditions osteoarthritis, adult Respiratory Distress Syndrome, Respiratory Distress Syndrome of infancy, ischemia reperfusion injury, glomerulonephritis, and chronic obstructive pulmonary disease (COPD) allergic conditions, asthma and atopic dermatitis, inflammation associated with infection, viral inflammation, influenza, hepatitis and Guillain-Barre, chronic bronchitis, chronic or acute tissue, cell, and solid organ transplant rejection, xeno-transplantation, atherosclerosis, restenosis, HIV infectivity (co-receptor usage), and granulomatous diseases, sarcoidosis, leprosy and tuberculosis, and sequelae associated with cancers, multiple myeloma; limiting the production of cytokines and/or TNF at inflammatory sites, as a consequence of decreasing cell infiltration; for treating diseases and/or congestive heart failure, linked to TNF and IL-1 and for treating pulmonary emphysema or dyspnea associated therewith, emphysema; HIV-1, HIV-2, HIV-3; cytomegalovirus (CMV), adenoviruses, Herpes viruses (*Herpes zoster* and *Herpes simplex*), for treating sequelae associated with infection where such infection induces production of detrimental inflammatory cytokines and/or TNF, fungal meningitis, joint tissue damage, hyperplasia, pannus formation and bone resorption, psoriatic arthritis, hepatic failure, bacterial meningitis, Kawasaki syndrome, myocardial infarction, acute liver failure, lyme disease, septic shock, cancer, trauma, and malaria, in a mammal, comprising an amount of a compound according to claim 20-~~or 24~~, or a pharmaceutically acceptable salt thereof, that is effective in treating or preventing such disorder or condition and a pharmaceutically acceptable carrier.

11. (Currently Amended) A pharmaceutical composition for treating or preventing a disorder or condition that can be treated or prevented by inhibiting chemokine binding to the receptor CCR1

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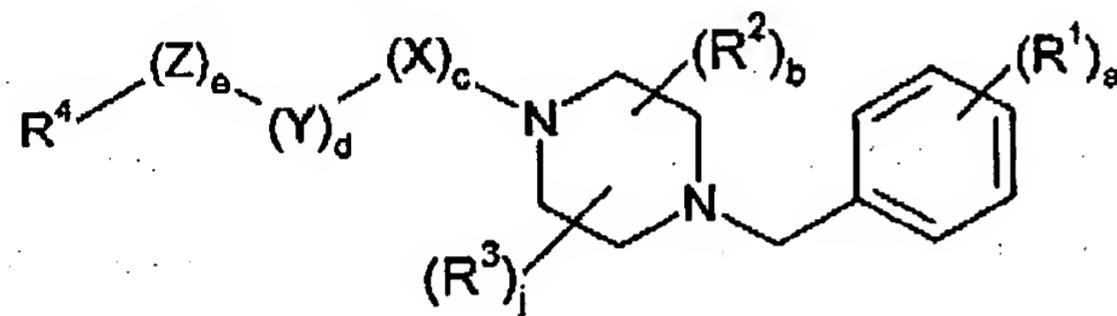
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in a mammal, comprising an amount of a compound according to claim 20-~~or~~21, or a pharmaceutically acceptable salt thereof, effective in treating or preventing such disorder or condition and a pharmaceutically acceptable carrier.

12-19. (Cancelled)

20. (Currently Amended) A compound of the formula



or the pharmaceutically acceptable salt thereof; wherein

R^1 is independently selected from hydrogen, halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, (C_1-C_6) alkyl, hydroxy or (C_1-C_6) alkylcarbonyloxy; R^2 and R^3 are each independently selected from (C_1-C_6) alkyl, (C_3-C_8) cycloalkyl, amino(C_1-C_6)alkyl, amino(C_3-C_8)cycloalkyl, (C_1-C_6) alkylamino(C_1-C_6)alkyl, (C_1-C_6) alkylamino(C_3-C_8)cycloalkyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6) alkoxycarbonylamino(C_1-C_6)alkyl, ureido(C_1-C_6)alkyl, (C_1-C_6)alkyureido(C_1-C_6)alkyl, (C_2-C_9) heteroaryl(C_1-C_6)alkyl or (C_2-C_9) heterocycloalkyl(C_1-C_6)alkyl;

R^4 is $(R^5)_f(R^6)_g(C_6-C_{10})$ aryl or $(R^5)_h(R^7)_k(C_2-C_9)$ heteroaryl wherein f, g and h are independently 1 or 2;

R^5 is (C_2-C_9) heterocycloalkylcarbonyl, (C_2-C_9) heteroarylcarbonyl, (C_2-C_9) heteroaryl(C_1-C_6)alkylaminocarbonyl, (C_2-C_9) heterocycloalkyl(C_1-C_6)alkylaminocarbonyl, (C_1-C_6) alkylsulfonylamino(C_1-C_6)alkylaminocarbonyl, ureido(C_1-C_6)alkylaminocarbonyl, (C_1-C_6) alkylureido(C_1-C_6)alkylaminocarbonyl, $((C_1-C_6)$ alkyl)2ureido(C_1-C_6)alkylaminocarbonyl, aminosulfonyl(C_1-C_6)alkylaminocarbonyl, (C_1-C_6) alkylaminosulfonyl(C_1-C_6)alkylaminocarbonyl, (C_1-C_6) alkylsulfonylamino(C_1-C_6)alkylcarbonylamino, cyanoguanidino(C_1-C_6)alkylcarbonylamino, (C_1-C_6) alkylcyanoguanidino(C_1-C_6)alkylcarbonylamino, $((C_1-C_6)$ alkyl)2cyanoguanidino(C_1-C_6)alkylcarbonylamino, aminocarbonyl(C_1-C_6)alkylcarbonylamino, (C_2-C_9) heteroaryl(C_1-C_6)alkylcarbonylamino,

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(C₁-C₆)alkylcarbonylamino, (C₂-C₉)heterocycloalkyl(C₁-C₆)alkylcarbonylamino, aminosulfonyl(C₁-C₆)alkylcarbonylamino, amino(C₁-C₆)alkylureido, (C₁-C₆)alkylamino(C₁-C₆)alkylureido, ((C₁-C₆)alkyl)₂amino(C₁-C₆)alkylureido, (C₂-C₉)heterocycloalkyl(C₁-C₆)alkylureido, (C₂-C₉)heteroaryl(C₁-C₆)alkylureido, aminosulfonyl(C₁-C₆)alkylureido, aminocarbonyl(C₁-C₆)alkylureido, (C₁-C₆)alkylaminocarbonyl(C₁-C₆)alkylureido, ((C₁-C₆)alkyl)₂aminocarbonyl(C₁-C₆)alkylureido, acetylamino(C₁-C₆)alkylureido, (acetyl)((C₁-C₆)alkyl)amino(C₁-C₆)alkylureido, amino(C₁-C₆)alkylsulfonylamino, (C₁-C₆)alkylamino(C₁-C₆)alkylsulfonylamino, ((C₁-C₆)alkyl)₂amino(C₁-C₆)alkylsulfonylamino, acetylamino(C₁-C₆)alkylsulfonylamino, (acetyl)((C₁-C₆)alkyl)amino(C₁-C₆)alkylsulfonylamino, ureido(C₁-C₆)alkylsulfonylamino, (C₁-C₆)alkylureido(C₁-C₆)alkylsulfonylamino, ((C₁-C₆)alkyl)₂ureido(C₁-C₆)alkylsulfonylamino, (C₁-C₆)alkylsulfonylamino(C₁-C₆)alkylsulfonylamino, cyanoguanidino(C₁-C₆)alkylsulfonylamino, (C₁-C₆)alkylcyanoguanidino(C₁-C₆)alkylsulfonylamino, ((C₁-C₆)alkyl)₂cyanoguanidino(C₁-C₆)alkylsulfonylamino, aminocarbonyl(C₁-C₆)alkylsulfonylamino, (C₁-C₆)alkoxycarbonylamino(C₁-C₆)alkylsulfonylamino, aminosulfonylamino, (C₁-C₆)alkylaminosulfonylamino, ((C₁-C₆)alkyl)₂aminosulfonylamino, aminocarbonyl(C₁-C₆)alkylamino(C₁-C₆)alkylsulfonylamino, (C₂-C₉)heterocycloalkyloxycarbonylamino(C₁-C₆)alkylsulfonylamino, (C₂-C₉)heteroaryloxycarbonylamino(C₁-C₆)alkylsulfonylamino, cyanoguanidino, (C₁-C₆)alkylcyanoguanidino, ((C₁-C₆)alkyl)₂cyanoguanidino, (C₂-C₉)heterocycloalkylcyanoguanidino, (C₂-C₉)heteroarylcyanoguanidino, (C₂-C₉)heterocycloalkyl(C₁-C₆)alkylcyanoguanidino, (C₂-C₉)heteroaryl(C₁-C₆)alkylcyanoguanidino, amino(C₁-C₆)alkylcyanoguanidino, (C₁-C₆)alkylcyanoguanidino, (C₁-C₆)alkylamino(C₁-C₆)alkylcyanoguanidino, ((C₁-C₆)alkyl)₂amino(C₁-C₆)alkylcyanoguanidino, aminocarbonyl(C₁-C₆)alkylcyanoguanidino, (C₁-C₆)alkylaminocarbonyl(C₁-C₆)alkylcyanoguanidino, ((C₁-C₆)alkyl)₂aminocarbonyl(C₁-C₆)alkylcyanoguanidino, aminocarbonyl(C₁-C₆)alkylamino, (C₁-C₆)alkylsulfonylamino(C₁-C₆)alkylamino, (C₁-C₆)alkylamino(C₁-C₆)alkylamino, aminosulfonyl(C₁-C₆)alkylamino, (C₂-C₉)heteroaryl(C₁-C₆)alkylamino, acetylamino(C₁-C₆)alkylamino, (acetyl)((C₁-C₆)alkyl)amino(C₁-C₆)alkylamino, cyano(C₁-C₆)alkylaminoalkyl, aminocarbonyl(C₁-C₆)alkylamino(C₁-C₆)alkyl, acetylamino(C₁-C₆)alkylamino(C₁-C₆)alkyl, (acetyl)((C₁-C₆)alkyl)amino(C₁-C₆)alkylamino(C₁-C₆)alkyl, (C₁-C₆)alkoxycarbonylamino(C₁-C₆)alkylamino(C₁-C₆)alkyl,

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(C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, (C₁-C₆)alkyl(cyanoguanidino)(C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, ((C₁-C₆)alkyl)₂(cyanoguanidino)(C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, aminocarbonyl(C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, (C₁-C₆)alkoxycarbonylamino(C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, (C₂-C₉)heterocycloalkyloxycarbonylamino(C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, (C₂-C₉)heteroaryloxycarbonylamino(C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, aminosulfonylamino(C₁-C₆)alkyl, (C₁-C₆)alkylaminosulfonylamino(C₁-C₆)alkyl, ((C₁-C₆)alkyl)₂aminosulfonylamino(C₁-C₆)alkyl, cyanoguanidino(C₁-C₆)alkyl, (C₁-C₆)alkyl(cyanoguanidino)(C₁-C₆)alkyl, ((C₁-C₆)alkyl)₂(cyanoguanidino)(C₁-C₆)alkyl, (C₂-C₉)heterocycloalkyl(cyanoguanidino)(C₁-C₆)alkyl, (C₂-C₉)heteroaryl(cyanoguanidino)(C₁-C₆)alkyl, (C₂-C₉)heterocycloalkyl(C₁-C₆)alkyl(cyanoguanidino)(C₁-C₆)alkyl, (C₂-C₉)heteroaryl(C₁-C₆)alkyl(cyanoguanidino)(C₁-C₆)alkyl, amino(C₁-C₆)alkyl(cyanoguanidino)(C₁-C₆)alkyl, (C₁-C₆)alkylaminocarbonyl(C₁-C₆)alkyl(cyanoguanidino)(C₁-C₆)alkyl, ((C₁-C₆)alkyl)₂aminocarbonyl(C₁-C₆)alkyl(cyanoguanidino)(C₁-C₆)alkyl, (C₁-C₆)alkylaminosulfonyl, (C₁-C₆)alkylaminosulfonyl, ((C₁-C₆)alkyl)₂amino(C₁-C₆)alkylaminosulfonyl, (C₁-C₆)alkylaminosulfonyl, (C₂-C₉)heteroarylamino(C₁-C₆)alkylaminosulfonyl, ureido(C₁-C₆)alkylaminosulfonyl, (C₁-C₆)alkylureido(C₁-C₆)alkylaminosulfonyl, ((C₁-C₆)alkyl)₂ureido(C₁-C₆)alkylaminosulfonyl, (C₁-C₆)alkylsulfonylamino(C₁-C₆)alkylaminosulfonyl, (C₁-C₆)alkoxycarbonylamino(C₁-C₆)alkylaminosulfonyl, (C₂-C₉)heterocycloalkyloxycarbonylamino(C₁-C₆)alkylaminosulfonyl, (C₁-C₆)heteroaryloxycarbonylamino(C₁-C₆)alkylaminosulfonyl, aminocarbonyl(C₁-C₆)alkylaminosulfonyl, cyanoguanidino(C₁-C₆)alkylaminosulfonyl, (C₂-C₉)heteroaryl(C₁-C₆)alkylaminosulfonyl, (C₂-C₉)heterocycloalkylaminosulfonyl, halo(C₁-C₆)alkylaminocarbonyl, hydroxy(C₁-C₆)alkylureido, halo(C₁-C₆)alkylsulfonylamino, (C₁-C₆)alkoxycarbonyl(C₁-C₆)alkylaminocarbonyl, hydroxy(C₁-C₆)alkylaminocarbonyl(C₁-C₆)alkyl, halo(C₁-C₆)alkylaminocarbonyl(C₁-C₆)alkyl, hydroxy(C₁-C₆)alkylaminosulfonyl, (C₁-C₆)alkylaminosulfonyl, ((C₁-C₆)alkyl)₂aminosulfonyl, hydroxy(C₁-C₆)alkylaminosulfonyl, or (C₁-C₆)alkoxy(C₁-C₆)alkylaminosulfonyl;

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R^6 and R^7 are each independently halo, halo(C_1 - C_6)alkyl, (C_1 - C_6)alkyl, (C_1 - C_6)alkoxy, trifluoromethyl, trifluoromethoxy, hydroxy, aminocarbonyl, cyano, ureido, (C_1 - C_6)alkylsulfonylamino, (C_1 - C_6)alkoxycarbonylamino or glycaminino;

a is 1, 2, 3, 4 or 5;

b is 0, 1, 2, 3 or 4;

c is 1;

d is 1;

e is 1;

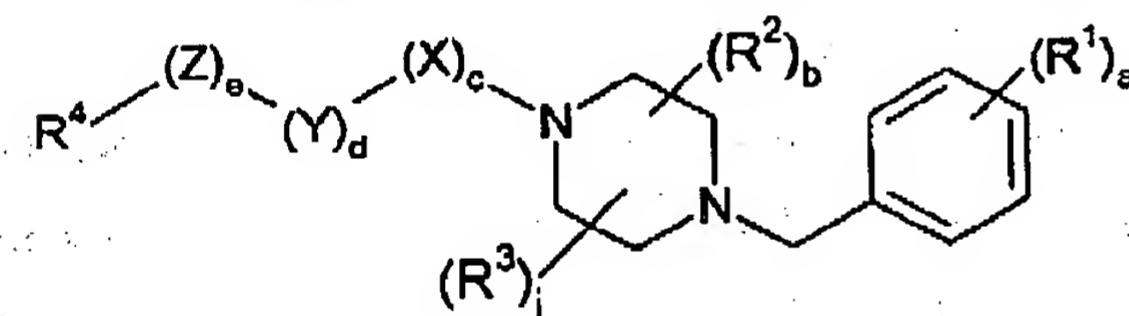
j is 1, 2, 3, or 4;

Y is CH_2 ;

X is $C(O)$; and

Z is oxygen.

21. (Withdrawn) A compound of the formula



or the pharmaceutically acceptable salt thereof; wherein

R^1 is hydrogen, halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, (C_1 - C_6)alkyl, hydroxy or (C_1 - C_6)alkylcarbonyloxy;

R^2 and R^3 are each independently selected from (C_1 - C_6)alkyl, (C_3 - C_8)cycloalkyl, amino(C_1 - C_6)alkyl, amino(C_3 - C_8)cycloalkyl, (C_1 - C_6)alkylamino(C_1 - C_6)alkyl, (C_1 - C_6)alkylamino(C_3 - C_8)cycloalkyl, hydroxy(C_1 - C_6)alkyl, (C_1 - C_6)alkoxycarbonylamino(C_1 - C_6)alkyl, ureido(C_1 - C_6)alkyl, (C_1 - C_6)alkylureido(C_1 - C_6)alkyl, (C_2 - C_9)heteroaryl(C_1 - C_6)alkyl or (C_2 - C_9)heterocycloalkyl(C_1 - C_6)alkyl;

R^4 is $(R^5)_f(R^6)_g(C_6$ - $C_{10})$ aryl or $(R^5)_f(R^7)_h(C_2$ - $C_9)$ heteroaryl wherein f , g and h are independently 1 or 2;

R^5 is (C_2 - C_9)heterocycloalkylcarbonyl, (C_2 - C_9)heteroarylcarbonyl, (C_2 - C_9)heteroaryl(C_1 -

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C₆)alkylaminocarbonyl(C₁-C₆)alkylcyanoguanidino, ((C₁-C₆)alkyl)₂aminocarbonyl(C₁-C₆)alkylcyanoguanidino, aminocarbonyl(C₁-C₆)alkylamino, (C₁-C₆)alkylsulfonylamino(C₁-C₆)alkylamino, (C₁-C₆)alkoxycarbonylamino(C₁-C₆)alkylamino, aminosulfonyl(C₁-C₆)alkylamino, (C₂-C₉)heteroaryl(C₁-C₆)alkylamino, acetyl amino(C₁-C₆)alkylamino, (acetyl)((C₁-C₆)alkyl)amino(C₁-C₆)alkylamino, cyano(C₁-C₆)alkylaminoalkyl, aminocarbonyl(C₁-C₆)alkylamino(C₁-C₆)alkyl, acetyl amino(C₁-C₆)alkylamino(C₁-C₆)alkyl, (acetyl)((C₁-C₆)alkyl)amino(C₁-C₆)alkylamino(C₁-C₆)alkyl, (C₁-C₆)alkoxycarbonylamino(C₁-C₆)alkylamino(C₁-C₆)alkyl, (C₂-C₉)heterocycloalkyloxycarbonylamino(C₁-C₆)alkylamino(C₁-C₆)alkyl, cyanoguanidino(C₁-C₆)alkylamino(C₁-C₆)alkyl, (C₁-C₆)alkylcyanoguanidino(C₁-C₆)alkylamino(C₁-C₆)alkyl, ((C₁-C₆)alkyl)₂cyanoguanidino(C₁-C₆)alkylamino(C₁-C₆)alkyl, (C₁-C₆)alkylsulfonylamino(C₁-C₆)alkylamino(C₁-C₆)alkyl, ureido(C₁-C₆)alkylamino(C₁-C₆)alkyl, (C₁-C₆)alkylureido(C₁-C₆)alkylamino(C₁-C₆)alkyl, ((C₁-C₆)alkyl)₂ureido(C₁-C₆)alkylamino(C₁-C₆)alkyl, aminocarbonyloxy(C₁-C₆)alkylamino(C₁-C₆)alkyl, acetyl amino(C₁-C₆)alkylcarbonylamino(C₁-C₆)alkyl, (acetyl)((C₁-C₆)alkyl)amino(C₁-C₆)alkylcarbonylamino(C₁-C₆)alkyl, aminocarbonyl(C₁-C₆)alkylcarbonylamino(C₁-C₆)alkyl, (C₁-C₆)alkylaminocarbonyl(C₁-C₆)alkylcarbonylamino(C₁-C₆)alkyl, ((C₁-C₆)alkyl)₂aminocarbonyl(C₁-C₆)alkylcarbonylamino(C₁-C₆)alkyl, aminosulfonyl(C₁-C₆)alkylcarbonylamino(C₁-C₆)alkyl, (C₂-C₉)heterocycloalkyloxycarbonylamino(C₁-C₆)alkyl, cyanoguanidino(C₁-C₆)alkylcarbonylamino(C₁-C₆)alkyl, cyano(C₁-C₆)alkylcarbonylamino(C₁-C₆)alkyl, wherein R⁵ is amino(C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, (C₁-C₆)alkylamino(C₁-C₆)alkylaminocarbonyl amino(C₁-C₆)alkyl, ((C₁-C₆)alkyl)₂amino(C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, aminocarbonyl(C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, (C₁-C₆) alkylcarbonylamino(C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, (C₁-C₆)alkylsulfonylamino(C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, (C₁-C₆)alkoxycarbonyl amino(C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, (C₂-C₉)heterocycloalkyloxycarbonyl amino(C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, (C₂-C₉)heteroaryloxycarbonylamino(C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, (C₂-C₉)heteroaryl(C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, ureido(C₁-C₆)alkylureido(C₁-C₆)alkyl, (C₁-C₆)alkylureido(C₁-C₆)alkyl, ((C₁-C₆)alkyl)₂ureido(C₁-C₆)alkyl,

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C_6)alkyl $_2$ ureido(C_1 - C_6)alkylureido(C_1 - C_6)alkyl or cyanoguanidino(C_1 - C_6)alkylureido(C_1 - C_6)alkyl, amino(C_1 - C_6)alkylsulfonylamino(C_1 - C_6)alkyl, (C_1 - C_6)alkylamino(C_1 - C_6)alkylsulfonylamino(C_1 - C_6)alkyl, ((C_1 - C_6)alkyl) $_2$ amino(C_1 - C_6)alkylsulfonylamino(C_1 - C_6)alkyl, acetylamino(C_1 - C_6)alkylsulfonylamino(C_1 - C_6)alkyl, (acetyl)((C_1 - C_6)alkyl)amino(C_1 - C_6)alkylsulfonylamino(C_1 - C_6)alkyl, ureido(C_1 - C_6)alkylsulfonylamino(C_1 - C_6)alkyl, (C_1 - C_6)alkylureido(C_1 - C_6)alkylsulfonylamino(C_1 - C_6)alkyl, ((C_1 - C_6)alkyl) $_2$ ureido(C_1 - C_6)alkylsulfonylamino(C_1 - C_6)alkyl, (C_1 - C_6)alkylsulfonylamino(C_1 - C_6)alkylsulfonylamino(C_1 - C_6)alkyl, cyanoguanidino(C_1 - C_6)alkylsulfonylamino(C_1 - C_6)alkyl, (C_1 - C_6)alkyl(cyanoguanidino)(C_1 - C_6)alkylsulfonylamino(C_1 - C_6)alkyl, ((C_1 - C_6)alkyl) $_2$ (cyanoguanidino)(C_1 - C_6)alkylsulfonylamino(C_1 - C_6)alkyl, aminocarbonyl(C_1 - C_6)alkylsulfonylamino(C_1 - C_6)alkyl, (C_1 - C_6)alkoxycarbonylamino(C_1 - C_6)alkylsulfonylamino(C_1 - C_6)alkyl, (C_2 - C_9)heterocycloalkyloxycarbonylamino(C_1 - C_6)alkylsulfonylamino(C_1 - C_6)alkyl, (C_2 - C_9)heteroaryloxycarbonylamino(C_1 - C_6)alkylsulfonylamino(C_1 - C_6)alkyl, aminosulfonylamino(C_1 - C_6)alkyl, (C_1 - C_6)alkylaminosulfonylamino(C_1 - C_6)alkyl, ((C_1 - C_6)alkyl) $_2$ aminosulfonylamino(C_1 - C_6)alkyl, cyanoguanidino(C_1 - C_6)alkyl, (C_1 - C_6)alkyl(cyanoguanidino)(C_1 - C_6)alkyl, ((C_1 - C_6)alkyl) $_2$ (cyanoguanidino)(C_1 - C_6)alkyl, (C_2 - C_9)heterocycloalkyl(cyanoguanidino)(C_1 - C_6)alkyl, (C_2 - C_9)heteroaryl(cyanoguanidino)(C_1 - C_6)alkyl, (C_2 - C_9)heterocycloalkyl(C_1 - C_6)alkyl(cyanoguanidino)(C_1 - C_6)alkyl, (C_2 - C_9)heteroaryl(C_1 - C_6)alkyl(cyanoguanidino)(C_1 - C_6)alkyl, (C_2 - C_9)heteroaryl(C_1 - C_6)alkyl(cyanoguanidino)(C_1 - C_6)alkyl, amino(C_1 - C_6)alkyl(cyanoguanidino)(C_1 - C_6)alkyl, (C_1 - C_6)alkylamino(C_1 - C_6)alkyl(cyanoguanidino)(C_1 - C_6)alkyl, ((C_1 - C_6)alkyl) $_2$ amino(C_1 - C_6)alkyl(cyanoguanidino)(C_1 - C_6)alkyl, aminocarbonyl(C_1 - C_6)alkyl(cyanoguanidino)(C_1 - C_6)alkyl, (C_1 - C_6)alkylaminocarbonyl(C_1 - C_6)alkyl(cyanoguanidino)(C_1 - C_6)alkyl, ((C_1 - C_6)alkyl) $_2$ aminocarbonyl(C_1 - C_6)alkyl(cyanoguanidino)(C_1 - C_6)alkyl, wherein R^5 is (C_2 - C_9)heterocycloalkylsulfonyl, amino(C_1 - C_6)alkylaminosulfonyl, (C_1 - C_6)alkylamino(C_1 - C_6)alkylaminosulfonyl, ((C_1 - C_6)alkyl) $_2$ amino(C_1 - C_6)alkylaminosulfonyl, (C_2 - C_9)heteroarylaminosulfonyl, ureido(C_1 - C_6)alkylaminosulfonyl, (C_1 - C_6)alkylureido(C_1 - C_6)alkylaminosulfonyl, ((C_1 - C_6)alkyl) $_2$ ureido(C_1 - C_6)alkylaminosulfonyl, (C_1 - C_6)alkylsulfonylamino(C_1 - C_6)alkylaminosulfonyl, (C_1 - C_6)alkoxycarbonylamino(C_1 - C_6)alkylaminosulfonyl, (C_2 - C_9)heterocycloalkyloxycarbonylamino(C_1 - C_6)alkylaminosulfonyl, (C_2 - C_9)heteroaryloxycarbonylamino(C_1 - C_6)alkylaminosulfonyl, aminocarbonyl(C_1 - C_6)alkylaminosulfonyl,

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(C_1-C_6) alkylaminosulfonyl, cyanoguanidino (C_1-C_6) alkylaminosulfonyl, (C_2-C_9) heteroaryl (C_1-C_6) alkylaminosulfonyl, (C_2-C_9) heterocycloalkylaminosulfonyl, halo (C_1-C_6) alkylaminocarbonyl, hydroxy (C_1-C_6) alkylureido, halo (C_1-C_6) alkylsulfonylamino, (C_1-C_6) alkoxycarbonyl (C_1-C_6) alkylamino (C_1-C_6) alkyl, hydroxy (C_1-C_6) alkylaminocarbonylamino (C_1-C_6) alkyl, halo (C_1-C_6) alkylsulfonylamino (C_1-C_6) alkyl, aminosulfonyl, (C_1-C_6) alkylaminosulfonyl, $((C_1-C_6)$ alkyl $)_2$ aminosulfonyl, hydroxy (C_1-C_6) alkylaminosulfonyl, or (C_1-C_6) alkoxy (C_1-C_6) alkylaminosulfonyl;

R^6 and R^7 are each independently halo, halo (C_1-C_6) alkyl, (C_1-C_6) alkyl, (C_1-C_6) alkoxy, trifluoromethyl, trifluoromethoxy, hydroxy, aminocarbonyl, cyano, ureido, (C_1-C_6) alkylsulfonylamino, (C_1-C_6) alkoxycarbonylamino or glycaminino;

a is 1, 2, 3, 4 or 5;

b is 0, 1, 2, 3 or 4;

c is 1;

d is 1;

e is 1;

j is 1, 2, 3, or 4;

Y is CH_2 ;

X is $C(O)$; and

Z is NR^9 wherein R^9 is hydrogen or (C_1-C_6) alkyl.

22. (Currently Amended) The compound of claim 20 or 21 wherein R^5 is (C_2-C_9) heterocycloalkylcarbonyl, (C_2-C_9) heteroarylcarbonyl, (C_2-C_9) heteroaryl (C_1-C_6) alkylaminocarbonyl, (C_2-C_9) heterocycloalkyl (C_1-C_6) alkylaminocarbonyl, (C_1-C_6) alkylsulfonylamino (C_1-C_6) alkylaminocarbonyl, ureido (C_1-C_6) alkylaminocarbonyl, (C_1-C_6) alkylureido (C_1-C_6) alkylaminocarbonyl, $((C_1-C_6)$ alkyl $)_2$ ureido (C_1-C_6) alkylaminocarbonyl, aminosulfonyl (C_1-C_6) alkylaminocarbonyl or (C_1-C_6) alkylaminosulfonyl (C_1-C_6) alkylaminocarbonyl.

23. (Currently Amended) The compound of claim 20 or 21 wherein R^5 is (C_1-C_6) alkylsulfonylamino (C_1-C_6) alkylcarbonylamino, cyanoguanidino (C_1-C_6) alkylcarbonylamino, (C_1-C_6)

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C_6)alkylcyanoguanidino(C_1 - C_6)alkylcarbonylamino, $((C_1$ - C_6)alkyl) $_2$ cyanoguanidino(C_1 - C_6)alkylcarbonylamino, aminocarbonyl(C_1 - C_6)alkylcarbonylamino, (C_2 - C_9)heteroaryl(C_1 - C_6)alkylcarbonylamino, (C_2 - C_9)heterocycloalkyl(C_1 - C_6)alkylcarbonylamino, or aminosulfonyl(C_1 - C_6)alkylcarbonylamino.

24. (Currently Amended) The compound of claim 20 or 21 wherein R^5 is amino(C_1 - C_6)alkylureido, (C_1 - C_6)alkylamino(C_1 - C_6)alkylureido, $((C_1$ - C_6)alkyl) $_2$ amino(C_1 - C_6)alkylureido, (C_2 - C_9)heterocycloalkyl(C_1 - C_6)alkylureido, (C_2 - C_9)heteroaryl(C_1 - C_6)alkylureido, aminosulfonyl(C_1 - C_6)alkylureido, aminocarbonyl(C_1 - C_6)alkylureido, (C_1 - C_6)alkylaminocarbonyl(C_1 - C_6)alkylureido, $((C_1$ - C_6)alkyl) $_2$ aminocarbonyl(C_1 - C_6)alkylureido, acetylamino(C_1 - C_6)alkylureido, or (acetyl)((C_1 - C_6)alkyl)amino(C_1 - C_6)alkylureido.

25. (Currently Amended) The compound of claim 20 or 21 wherein R^5 is amino(C_1 - C_6)alkylsulfonylamino, (C_1 - C_6)alkylamino(C_1 - C_6)alkylsulfonylamino, $((C_1$ - C_6)alkyl) $_2$ amino(C_1 - C_6)alkylsulfonylamino, acetylamino(C_1 - C_6)alkylsulfonylamino, (acetyl)((C_1 - C_6)alkyl)amino(C_1 - C_6)alkylsulfonylamino, ureido(C_1 - C_6)alkylsulfonylamino, (C_1 - C_6)alkylureido(C_1 - C_6)alkylsulfonylamino, $((C_1$ - C_6)alkyl) $_2$ ureido(C_1 - C_6)alkylsulfonylamino, (C_1 - C_6)alkylsulfonylamino(C_1 - C_6)alkylsulfonylamino, cyanoguanidino(C_1 - C_6)alkylsulfonylamino, (C_1 - C_6)alkylcyanoguanidino(C_1 - C_6)alkylsulfonylamino, $((C_1$ - C_6)alkyl) $_2$ cyanoguanidino(C_1 - C_6)alkylsulfonylamino, aminocarbonyl(C_1 - C_6)alkylsulfonylamino, (C_1 - C_6)alkoxycarbonylamino(C_1 - C_6)alkylsulfonylamino, aminosulfonylamino, (C_1 - C_6)alkylaminosulfonylamino, $((C_1$ - C_6)alkyl) $_2$ aminosulfonylamino, aminocarbonyl(C_1 - C_6)alkylamino(C_1 - C_6)alkylsulfonylamino, (C_2 - C_9)heterocycloalkyloxycarbonylamino(C_1 - C_6)alkylsulfonylamino or (C_2 - C_9)heteroaryloxycarbonylamino(C_1 - C_6)alkylsulfonylamino.

26. (Currently Amended) The compound of claim 20 or 21 wherein R^5 is cyanoguanidino, (C_1 - C_6)alkylcyanoguanidino, $((C_1$ - C_6)alkyl) $_2$ cyanoguanidino, (C_2 - C_9)heterocycloalkylcyanoguanidino, (C_2 - C_9)heteroarylcyanoguanidino, (C_2 - C_9)heterocycloalkyl(C_1 - C_6)alkylcyanoguanidino, (C_2 - C_9)heteroaryl(C_1 - C_6)alkylcyanoguanidino, amino(C_1 - C_6)alkylcyanoguanidino, (C_1 - C_6)

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C_6)alkylamino(C_1 - C_6)alkylcyanoguanidino, $((C_1$ - C_6)alkyl $)_2$ amino(C_1 - C_6)alkylcyanoguanidino, aminocarbonyl(C_1 - C_6)alkylcyanoguanidino, (C_1 - C_6)alkylaminocarbonyl(C_1 - C_6)alkylcyanoguanidino or $((C_1$ - C_6)alkyl $)_2$ aminocarbonyl(C_1 - C_6)alkylcyanoguanidino, wherein R^5 is aminocarbonyl(C_1 - C_6)alkylamino, (C_1 - C_6)alkylsulfonylamino(C_1 - C_6)alkylamino, (C_1 - C_6)alkoxycarbonylamino(C_1 - C_6)alkylamino, aminosulfonyl(C_1 - C_6)alkylamino, (C_2 - C_9)heteroaryl(C_1 - C_6)alkylamino, acetylamino(C_1 - C_6)alkylamino or (acetyl) $((C_1$ - C_6)alkyl)amino(C_1 - C_6)alkylamino.

27. (Currently Amended) The compound of claim 20 or 21 wherein R^5 is cyano(C_1 - C_6)alkylaminoalkyl or aminocarbonyl(C_1 - C_6)alkylamino(C_1 - C_6)alkyl.

28. (Currently Amended) The compound of claim 20 or 21 wherein R^5 is acetylamino(C_1 - C_6)alkylamino(C_1 - C_6)alkyl, (acetyl) $((C_1$ - C_6)alkyl)amino(C_1 - C_6)alkylamino(C_1 - C_6)alkyl, (C_1 - C_6)alkoxycarbonylamino(C_1 - C_6)alkylamino(C_1 - C_6)alkyl, (C_2 - C_9)heterocycloalkyloxycarbonylamino(C_1 - C_6)alkylamino(C_1 - C_6)alkyl, (C_2 - C_9)heteroaryloxycarbonylamino(C_1 - C_6)alkylamino(C_1 - C_6)alkyl, cyanoguanidino(C_1 - C_6)alkylamino(C_1 - C_6)alkyl, (C_1 - C_6)alkylcyanoguanidino(C_1 - C_6)alkylamino(C_1 - C_6)alkyl, ((C_1 - C_6)alkyl $)_2$ cyanoguanidino(C_1 - C_6)alkylamino(C_1 - C_6)alkyl, (C_1 - C_6)alkylsulfonylamino(C_1 - C_6)alkylamino(C_1 - C_6)alkyl, ureido(C_1 - C_6)alkylamino(C_1 - C_6)alkyl, (C_1 - C_6)alkylureido(C_1 - C_6)alkylamino(C_1 - C_6)alkyl, ((C_1 - C_6)alkyl $)_2$ ureido(C_1 - C_6)alkylamino(C_1 - C_6)alkyl or aminocarbonyloxy(C_1 - C_6)alkylamino(C_1 - C_6)alkyl.

29. (Currently Amended) The compound of claim 20 or 21 wherein R^5 is acetylamino(C_1 - C_6)alkylcarbonylamino(C_1 - C_6)alkyl, (acetyl) $((C_1$ - C_6)alkyl)amino(C_1 - C_6)alkylcarbonylamino(C_1 - C_6)alkyl, aminocarbonyl(C_1 - C_6)alkylcarbonylamino(C_1 - C_6)alkyl, (C_1 - C_6)alkylaminocarbonyl(C_1 - C_6)alkylcarbonylamino(C_1 - C_6)alkyl, ((C_1 - C_6)alkyl $)_2$ aminocarbonyl(C_1 - C_6)alkylcarbonylamino(C_1 - C_6)alkyl, aminosulfonyl(C_1 - C_6)alkylcarbonylamino(C_1 - C_6)alkyl, (C_2 - C_9)heterocycloalkyloxycarbonylamino(C_1 - C_6)alkyl, cyanoguanidino(C_1 - C_6)alkylcarbonylamino(C_1 - C_6)alkyl or cyano(C_1 - C_6)alkylcarbonylamino(C_1 - C_6)alkyl.

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30. (Currently Amended) The compound of claim 20 or 21 wherein R⁵ is amino(C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, (C₁-C₆)alkylamino(C₁-C₆)alkylaminocarbonyl amino(C₁-C₆)alkyl, ((C₁-C₆)alkyl)₂amino(C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, aminocarbonyl(C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, (C₁-C₆) alkylcarbonylamino(C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, (C₁-C₆)alkylsulfonylamino(C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, (C₁-C₆)alkoxycarbonyl amino(C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, (C₂-C₉)heterocycloalkyloxycarbonyl amino(C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, (C₂-C₉)heteroaryloxycarbonylamino(C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, (C₂-C₉)heterocycloalkyl(C₁-C₆)alkylaminocarbonyl amino(C₁-C₆)alkyl, (C₂-C₉)heteroaryl(C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, ureido(C₁-C₆)alkylureido(C₁-C₆)alkyl, (C₁-C₆)alkylureido(C₁-C₆)alkylureido(C₁-C₆)alkyl, ((C₁-C₆)alkyl)₂ureido(C₁-C₆)alkylureido(C₁-C₆)alkyl or cyanoguanidino(C₁-C₆)alkylureido(C₁-C₆)alkyl.

31. (Currently Amended) The compound of claim 20 or 21 wherein R⁵ is amino(C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, (C₁-C₆)alkylamino(C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, ((C₁-C₆)alkyl)₂amino(C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, acetylamino(C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, (acetyl)((C₁-C₆)alkyl)amino(C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, ureido(C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, (C₁-C₆)alkylureido(C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, ((C₁-C₆)alkyl)₂ureido(C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, (C₁-C₆)alkylsulfonylamino(C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, cyanoguanidino(C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, (C₁-C₆)alkyl(cyanoguanidino)(C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, ((C₁-C₆)alkyl)₂(cyanoguanidino)(C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, aminocarbonyl(C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, (C₁-C₆)alkoxycarbonylamino(C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, (C₂-C₉)heterocycloalkyloxycarbonylamino(C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, (C₂-C₉)heteroaryloxycarbonylamino(C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, aminosulfonylamino(C₁-C₆)alkyl, (C₁-C₆)alkylaminosulfonylamino(C₁-C₆)alkyl or ((C₁-C₆)alkyl)₂aminosulfonylamino(C₁-C₆)alkyl.

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32. (Currently Amended) The compound of claim 20 or 21 wherein R⁵ is cyanoguanidino(C₁-C₆)alkyl, (C₁-C₆)alkyl(cyanoguanidino)(C₁-C₆)alkyl, ((C₁-C₆)alkyl)₂(cyanoguanidino)(C₁-C₆)alkyl, (C₂-C₉)heterocycloalkyl(cyanoguanidino)(C₁-C₆)alkyl, (C₂-C₉)heteroaryl(cyanoguanidino)(C₁-C₆)alkyl, (C₂-C₉)heterocycloalkyl(C₁-C₆)alkyl(cyanoguanidino)(C₁-C₆)alkyl, (C₂-C₉)heteroaryl(C₁-C₆)alkyl(cyanoguanidino)(C₁-C₆)alkyl, amino(C₁-C₆)alkyl(cyanoguanidino)(C₁-C₆)alkyl, (C₁-C₆)alkylamino(C₁-C₆)alkyl(cyanoguanidino)(C₁-C₆)alkyl, ((C₁-C₆)alkyl)₂amino(C₁-C₆)alkyl(cyanoguanidino)(C₁-C₆)alkyl, aminocarbonyl(C₁-C₆)alkyl(cyanoguanidino)(C₁-C₆)alkyl, (C₁-C₆)alkylaminocarbonyl(C₁-C₆)alkyl(cyanoguanidino)(C₁-C₆)alkyl or ((C₁-C₆)alkyl)₂aminocarbonyl(C₁-C₆)alkyl(cyanoguanidino)(C₁-C₆)alkyl.

33. (Currently Amended) The compound of claim 20 or 21 wherein R⁵ is (C₂-C₉)heterocycloalkylsulfonyl, amino(C₁-C₆)alkylaminosulfonyl, (C₁-C₆)alkylamino(C₁-C₆)alkylaminosulfonyl, ((C₁-C₆)alkyl)₂amino(C₁-C₆)alkylaminosulfonyl, (C₂-C₉)heteroarylaminosulfonyl, ureido(C₁-C₆)alkylaminosulfonyl, (C₁-C₆)alkylureido(C₁-C₆)alkylaminosulfonyl, ((C₁-C₆)alkyl)₂ureido(C₁-C₆)alkylaminosulfonyl, (C₁-C₆)alkylsulfonylamino(C₁-C₆)alkylaminosulfonyl, (C₁-C₆)alkoxycarbonylamino(C₁-C₆)alkylaminosulfonyl, (C₂-C₉)heterocycloalkyloxycarbonylamino(C₁-C₆)alkylaminosulfonyl, (C₂-C₉)heteroaryloxycarbonylamino(C₁-C₆)alkylaminosulfonyl, aminocarbonyl(C₁-C₆)alkylaminosulfonyl, cyanoguanidino(C₁-C₆)alkylaminosulfonyl, (C₂-C₉)heteroaryl(C₁-C₆)alkylaminosulfonyl, (C₂-C₉)heterocycloalkylaminosulfonyl, Other preferred compounds of formula I include those wherein R⁵ is halo(C₁-C₆)alkylaminocarbonyl, hydroxy(C₁-C₆)alkylureido, halo(C₁-C₆)alkylsulfonylamino, (C₁-C₆)alkoxycarbonyl(C₁-C₆)alkylamino(C₁-C₆)alkyl, hydroxy(C₁-C₆)alkylaminocarbonyl(C₁-C₆)alkyl, halo(C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, aminosulfonyl, (C₁-C₆)alkylaminosulfonyl, ((C₁-C₆)alkyl)₂aminosulfonyl, hydroxy(C₁-C₆)alkylaminosulfonyl, and/or (C₁-C₆)alkoxy(C₁-C₆)alkylaminosulfonyl.